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First person – Mitro Miihkinen

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping early-career researchers promote themselves alongside their papers. Mitro Miihkinen is co-first author on 'ProLIF – quantitative integrin protein–protein interactions and synergistic membrane effects on proteoliposomes', published in the 'Reconstituting Cell Biology' special issue of Journal of Cell Science. Mitro is a PhD student in the lab of Johanna Ivaska at Turku Centre for Biotechnology, Turku, Finland, investigating the role of integrins and filopodia in cancer cell invasion.

How would you explain the main findings of your paper in lay terms?

Biological membranes serve as delimiters for all cells across the tree of life. Today, these membranes are also known as a key interface, where chemical and physical cues from outside the cell are transformed into complex signaling events, eventually dictating the cell's responses to these cues. Signaling events from the cell membrane are regulated by its lipid composition as well as by membrane-embedded proteins. Even though this concept of outside-in signaling is a critical process in cell biology, the tools to measure binding events in the context of biological membranes have remained underdeveloped. Our publication describes an assay (named ProLIF) where binding events to biological membranes with and without integral proteins can be measured in an accurate and quantitative way.

Were there any specific challenges associated with this project? If so, how did you overcome them?

Integrins are the main cell adhesion receptors. They are heterodimers of two subunits, each consisting of an extracellular domain, a single transmembrane domain and a small cytoplasmic tail responsible for recruiting intracellular machinery at sites of receptor activation. As the focus of our research is to understand integrin function, we wanted to reconstitute the integrin–cytoplasmic membrane interface by embedding transmembrane–cytoplasmic tail segments of integrins into lipid membranes and quantitatively measuring the binding of cytoplasmic integrin-associated proteins. The first challenges were technical and related to purification of membrane protein segments and their liposome incorporation. However, by far the biggest challenges were linked to biological mechanisms such as auto-inhibition of integrin-associated proteins influencing their integrin-binding affinity in the reconstituted system. This reveals how we still know very little about how different integrins bind to their respective cytoplasmic signaling molecules. There are many unanswered questions around this topic that, hopefully, can be studied further with the help of reconstituted systems like ProLIF.

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Mitro Miihkinen

When doing the research, did you have a particular result or 'eureka' moment that has stuck with you?

So far we have focused on proof-of-concept studies to validate ProLIF as a method. However, I am confident that reconstituted systems like ProLIF will offer means to shed light onto questions that have previously remained difficult to answer. By developing this assay, we have taken the first steps to studying integrin biology in the context of the plasma membrane, and that is really valuable.

"Even though we use ProLIF to look at integrin binding and for analyzing protein–lipid interactions, I think the ideology behind it can be extended."

Why did you choose Journal of Cell Science for your paper?

Our article is part of the 'Reconstituting Cell Biology' special issue of Journal of Cell Science. This issue is highly suitable for

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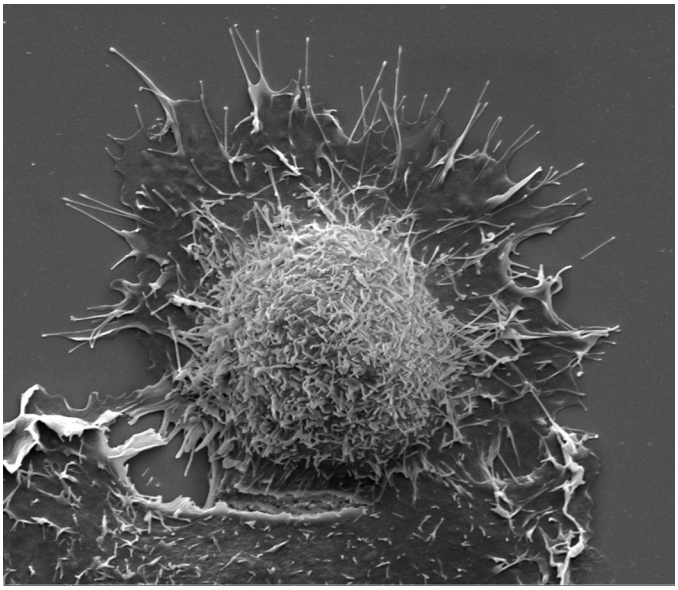

A cancer cell probes the surrounding matrix by extending multiple filopodia from the cell edges. By using extended filopodia together with its integrin receptors, the cell is able to establish new contacts with the extracellular matrix. During this process, a plethora of intracellular proteins bind to the integrin–cytoplasmic membrane interface to fine-tune cell adhesion. The current work describes a method (ProLIF) to probe these binding events. This scanning electron microscopy (EM) image is a part of a collaboration with Eija Jokitalo and Helena Vihinen at the University of Helsinki EM unit.

our work and it will hopefully catch a wide audience this way. Even though we use ProLIF to look at integrin binding and for analyzing protein–lipid interactions, I think the ideology behind it can be extended. Looking at other receptors embedded in lipid membranes or measuring the lipid-binding capabilities of protein domains in a more high-throughput setting are just a couple of options.

Have you had any significant mentors who have helped you beyond supervision in the lab?

In addition to collaborators and co-authors in the lab who have put their best efforts into this, I have received extremely valuable advice from all the people working in the Ivaska lab. These things highlight the key importance of collaboration in science.

What motivated you to pursue a career in science, and what have been the most interesting moments on the path that led you to where you are now?

In short, I was always the curious kid, so in a way pursuing a career in science was just something really natural for me to do. Once you get to do experiments and think about biology, you'll be able to make more and more sense out of it and that is really refreshing. For me, the best moments are the experiments where you realize something new about the system you're working with. If you get to test that idea and it turns out to be true, it is even better. In a way it's like seeing into the future.

> **"If you get to test that idea and it turns out to be true, it is even better. In a way it's like seeing into the future."**

Who are your role models in science? Why?

That is a big question. Many people are making great science in their respective fields. Whereas the collaborative efforts to create the cancer genome atlas (TCGA) has been really valuable for cancer biology, optogenetic tools now provide unprecedented accuracy to study the nervous system and it would be difficult to imagine a single idea with more transformative potential than artificial intelligence (AI) currently has. These are really exciting times. It's difficult to name a single person, but maybe my role model would be anyone who can come up with a solution to a tricky problem and is then able to actually see it through.

What's next for you?

I still need to work on my PhD for a little while, so I'm not in a hurry to decide anything yet. However, there are already a couple of things in mind that I could see myself doing in the future.

Tell us something interesting about yourself that wouldn't be on your CV

I'm somewhat addicted to sports and there's nothing as refreshing as a little jog or a swim after work. I'm also a huge foodie.

Reference

De Franceschi, N., Miihkinen, M., Hamidi, H., Alanko, J., Mai, A., Picas, L., Guzmán, C., Lévy, D., Mattjus, P., Goult, B. T. et al. (2019). ProLIF – quantitative integrin protein–protein interactions and synergistic membrane effects on proteoliposomes. *J. Cell Sci.* **131**, jcs214270.